

Amendments to the Specification:

Please amend the paragraph beginning on page 1, line 4 as follows:

This application is a divisional application of U.S. Application No. 10/358,835, filed February 5, 2003, now allowed, which claims the benefit of priority of U.S. Provisional Application No. 60/354,339 filed February 5, 2002, both of which are hereby incorporated by reference.

Please amend the paragraph beginning on page 21, line 6 as follows:

Another embodiment (5) of the invention is a compound according to any one of embodiments (1) to (2) wherein:

X is CH₂;

R¹ is H;

R² is methyl;

R³ and R⁴ are taken together form a 6-membered cyclic **morphine morpholine** ring.

Please amend the paragraph beginning on page 21, line 14 as follows:

Another embodiment (6) of the invention is a compound according to any one of embodiments (1) to (2) wherein:

X is CH₂;

R¹ is H;

R² is ethyl;

R³ and R⁴ are taken together form a 6-membered cyclic **morphine morpholine** ring.

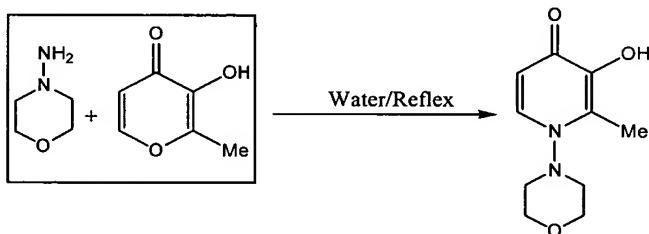
Please amend the paragraph beginning on page 35, line 12 as follows:

Materials. **4-Aminomorphine** **4-Aminomorpholine**, 1-aminopiperidine, ammonium chloride, benzoylhydrazine, ethylmaltol, isonicotinic acid hydrazide, maltol, nicotinic acid

hydrazide, phenylsulfonylhydrazide, sodium ascorbate, and thiophenecarboxylhydrazide were purchased from Aldrich, and were used as received. $^{111}\text{InCl}_3$ (in 0.05 N HCl) were purchased from NEN[®], N. Billerica, MA.

Please amend the paragraph beginning on page 36, line 19 as follows:

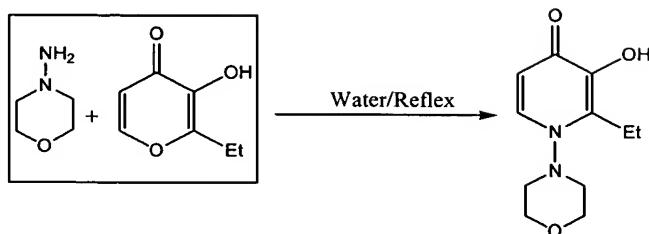
Example II - Synthesis of N-(1-Morphinyl)-2-Methyl-3-Hydroxy-4-Pyridinone N-(1-Morpholinyl)-2-Methyl-3-Hydroxy-4-Pyridinone (MMHP)



Maltol (3.6 g, 30 mmol) and 1-aminomorphine 1-aminomorpholine (4.5 g, 45 mmol) were suspended in 100 mL of water. The mixture was heated to reflux for 2 days to give a dark brown solution. The solvent was removed under vacuum to give a black residue. Upon standing at room temperature overnight, a solid was formed. The solid was collected by filtration and was then recrystallized in a mixture of water/methanol (2:1=v:v) to give brownish solid. The product was collected by filtration, washed with cold methanol, and dried under vacuum overnight. The yield was 0.60 g (~9.5%). LC-MS: $M/z = 211.2$ for $[\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_3]^+$. ^1H NMR (600 MHz, in CD_3OD , chemical shift in ppm relative to TMS): 2.50 (s, 3H, CH_3); 3.00 (d, 2H, $J_{\text{HH}} = 10.9$ mHz, $\text{CH}_2/\text{morphine}$ $\text{CH}_2/\text{morpholine}$); 3.29 (m, 2H, $\text{CH}_2/\text{morphine}$ $\text{CH}_2/\text{morpholine}$); 3.79 (m, 2H, $\text{CH}_2/\text{morphine}$ $\text{CH}_2/\text{morpholine}$); 4.00 (d, 2H, $\text{CH}_2/\text{morphine}$ $\text{CH}_2/\text{morpholine}$); 6.53 (d, 1H, $J_{\text{HH}} = 7.5$ mHz, $\text{CH}_2/\text{pyridinone}$); and 8.09 (d, 1H, $J_{\text{HH}} = 7.5$ mHz, CH/pyridinone).

Please amend the paragraph beginning on page 37, line 14 as follows:

Example III - Synthesis of N-(1-Morphinyl)-2-Ethyl-3-Hydroxy-4-Pyridinone N-(1-Morphinyl)-2-Ethyl-3-Hydroxy-4-Pyridinone (MEHP)



To a round-bottom flask were added ethylmaltol (3.2 g, 24 mmol), **1-aminomorphine** **1-aminomorpholine** (4.0 g, 40 mmol) and 100 mL of water. The mixture was heated to reflux for 2 days to give a dark brown solution. Upon removal of the solvent, the dark residue was re-dissolved in a mixture of hot water/methanol (50%:50% = v:v) in the presence of **charcoal**. The mixture was filtered while hot. Solvents were removed under vacuum to give a black residue. After standing at room temperature for 2 days, a solid was formed. The solid was collected by filtration and was then recrystallized in a mixture of water/methanol (2:1 = v:v) to give brownish microcrystals. The product was collected by filtration, washed with cold methanol, and dried under vacuum overnight. The yield was 0.48 g (~8.9%). LC-MS: $M/z = 225.3$ for $[C_{11}H_{16}N_2O_3]^+$. 1H NMR (600 MHz, in CD₃OD, chemical shift in ppm ~~relative~~ relative to TMS): 1.26 (t, 3H, CH₃); 2.95 (m, 4H, J_{HH} = CH₂/ethyl and morphine); 3.33 (m, 2H, CH₂/morphine); 3.80 (m, 2H, CH₂/morphine); 4.00 (m, 2H, CH₂/morphine); 6.49 (d, 1H, J_{HH} = 7.5 mHz, CH/pyridinone); and 8.05 (d, 1H, J_{HH} = 7.5 mHz, CH/pyridinone).